Evaluation Sample:

[0374] Compound K-1:J-1 was prepared as a 0.5 w/v % methylcellulose aqueous solution (0.5% MC, manufactured by FUJIFILM Wako Pure Chemical Corporation) at 5 mg/mL and intraperitoneally administered at 50 mg/kg per administration. 0.5% MC was administered to the negative control.

Procedure:

[0375] As the mouse, male C57BL/6NCrl, 6-week-old, was purchased from CHARLES RIVER LABORATORIES JAPAN, INC. As drinking water, distilled water or a 2.5 w/v % DSS aqueous solution was freely given. The DSS drinking start date was set as day 1, and the water was given until day 8. Compound K-1:J-1 was intraperitoneally administered at 50 mg/kg every 24 hr from day 1. On day 8, the mouse was dissected, the large intestine was isolated and the length of the large intestine was measured. Conducted in 4 cases in each group.

[0376] As the result of this test, FIG. **3** shows the length of the large intestine of the mouse. As shown in FIG. **3**, the large intestine of the DSS drinking water group was shorter than that of the distilled water drinking group. The shortening of the large intestine was suppressed more in the DSS drinking water-compound K-1:J-1 administration group than in the DSS drinking water-0.5% MC administration group. From the above, it was clarified that compound K-1:J-1 has an effect of suppressing the onset of DSS-derived colitis.

[Example 15] Wound Therapy Promoting Effect in Mouse Full-Thickness Skin Wound Model

[0377] A full-thickness skin wound in which the skin on the back of a mouse was partially removed was prepared as described below, and the wound therapy promoting effect of the compound was evaluated by comparing the reduction rate of the wound area.

Evaluation Sample:

[0378] Compound K-1:J-1 was dissolved in a solvent (10% Pluronic F-68, 2% Propylene Glycol, 20 mM Tris buffer (pH 8.5)) at a concentration of 1 mg/mL, and administered by adding dropwise to the wound site (0.04 mL per one wound site). To the negative control, the solvent alone was administered by dropwise addition.

Procedure:

[0379] As the mouse, male BKS.Cg-Dock7m+/+Leprdb/J, 7-week-old, was purchased from CHARLES RIVER LABORATORIES JAPAN, INC. After removing the hair on the back, an 8 mm full-thickness skin wound was prepared using biopsy trepan (Kai Corporation) and protected with a coating material (Tegaderm transparent dressing, 3M). The wound preparation date was set as day 1, and 1 mg/mL compound K-1:J-1 was added dropwise at a dose of 0.04 mL per wound site every 24 hr until day 12. The area of the wound site was measured on days 1, 3, 6, 9, 13. The wound area on day 1 was set to 100%, and the total measured area was calculated as a percentage (%) with respect to the wound preparation date. Conducted in 6 cases in each group.

[0380] As the result of this test, FIG. **4** shows changes in the wound area of the full-thickness skin wound model mouse. In addition, the area under the wound area ratio (Area Under the Curve (AUC), %×day) calculated from the result of the change over time of the wound area ratio was 854.2±119.2 in the negative control, and 659.6±163.7 in the K-1:J-1 administration group. As shown in FIG. **4** and AUC value, it was clarified that compound K-1:J-1 has a wound therapy promoting effect.

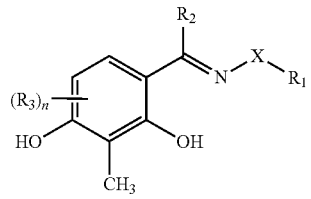
INDUSTRIAL APPLICABILITY

[0381] According to the present invention, it is possible to inhibit plural kinases including LATS (particularly LATS2) which is the major kinase in the Hippo signal transduction pathway. In addition, diseases or tissue damage associated with failure of cellular proliferation can be treated. Therefore, the present invention is beneficial, for example, in the research field of cell functions and diseases, in which the Hippo signal transduction pathway is involved, and the like. Furthermore, it is beneficial in the medical field for the treatment of such diseases and the like.

[0382] This application is based on patent application No. 2018-110748 filed in Japan (filing date: Jun. 8, 2018) and patent application No. 2019-014898 filed in Japan (filing date: Jan. 30, 2019), the contents of which are incorporated in full herein.

1. A kinase inhibitor comprising a compound represented by the following formula (I), or a salt thereof:

(I)



{wherein, X is a single bond, —CH_2COO—, —CONH—, or —NHCO—, R_1 is an alkyl group having 1-10 carbon atoms and optionally having substituent(s), an aryl group optionally having substituent(s), or —Y—W—Z—Ar wherein Y and Z are each a single bond or an alkylene group having 1-6 carbon atoms and optionally having substituent (s), W is an oxygen atom, a sulfur atom or $N(R_4)$, R_4 is a hydrogen atom or an alkyl group having 1-6 carbon atoms, Ar is an aryl group optionally having substituent(s), R_2 is an alkyl group having 1-6 carbon atoms and optionally having substituent(s), R_3 is a hydroxyl group, and n is 0, 1 or 2}.

2. The inhibitor according to claim **1**, wherein the kinase is selected from the group consisting of CGK2, LATS2, MSK1, p70S6K, PKACα, PKACβ, SGK2, and SGK3.

3. The inhibitor according to claim **2**, wherein the kinase is LATS2.

4. A Hippo signal transduction pathway inhibitor comprising a compound represented by the following formula (I) or a salt thereof: